Complete Summary

GUIDELINE TITLE

(1) Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack. (2) Update to the AHA/ASA recommendations for the prevention of stroke in patients with stroke and transient ischemic attack.

BIBLIOGRAPHIC SOURCE(S)

Adams RJ, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Sacco RL, Schwamm LH, American Heart Association, American Stroke Association. Update to the AHA/ASA recommendations for the prevention of stroke in patients with stroke and transient ischemic attack. Stroke 2008 May;39(5):1647-52. [10 references] PubMed

Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke [trunc]. Stroke 2006 Feb;37(2):577-617. [466 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Ischemic stroke
- Transient ischemic attack (TIA)

Note: The proposed new definition of TIA is a "brief episode of neurological dysfunction caused by a focal disturbance of brain or retinal ischemia, with clinical symptoms typically lasting less than 1 hour and without evidence of infarction."

GUIDELINE CATEGORY

Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine
Neurology
Preventive Medicine
Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

2006 Guideline

To provide comprehensive and timely evidence-based recommendations on the prevention of ischemic stroke among survivors of ischemic stroke or transient ischemic attack (TIA)

2008 Addendum

To provide a brief review of new data, to update specific recommendations, and to provide the reasons for any modifications

TARGET POPULATION

Patients with previous ischemic stroke or transient ischemic attack (TIA) including patients at high risk and pregnant women

INTERVENTIONS AND PRACTICES CONSIDERED

1. Risk factor control for all patients with transient ischemia attack (TIA) or ischemic stroke
    - Use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers for blood pressure control
    - Use of statins, gemfibrozil, and niacin for dyslipidemia
    - Control of blood glucose levels
    - Weight reduction, engaging in physical activity, smoking cessation, reduction in alcohol intake

2. Interventions in patients with stroke caused by large-artery stenosis
    - Carotid endarterectomy
    - Carotid artery balloon angioplasty and stenting
    - Extracranial/intracranial bypass surgery (considered but not recommended routinely)

3. Medical treatments for patients with cardiogenic embolism
    - Anticoagulation with adjusted-dose warfarin
    - Aspirin
    - Monitoring INR (international normalized ratio) during anticoagulation therapy

4. Antithrombotic therapy for noncardioembolic stroke or TIA
    - Antiplatelet agents (aspirin, ticlopidine, clopidogrel, dipyridamole alone or in combination)
    - Oral anticoagulants (considered but not recommended for noncardioembolic stroke or TIA)

5. Treatment for stroke patients with other specific conditions, including arterial dissections, patent foramen ovale, hyperhomocysteinemia, hypercoagulable states, sickle cell disease, cerebral venous sinus thrombosis, stroke among women (particularly in relation to pregnancy and the use of postmenopausal hormones), and the use of anticoagulation after cerebral hemorrhage

MAJOR OUTCOMES CONSIDERED

- Effectiveness of prevention strategies in the secondary prevention of stroke
- Effectiveness of treatment in risk reduction of vascular events and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

2006 Guideline

The writing committee reviewed all compiled reports from computerized searches and conducted additional searching by hand. Searches were limited to English language sources and to human subjects. Literature citations were generally restricted to published manuscripts appearing in journals listed in Index Medicus and reflected literature published as of December 31, 2004. Because of the scope and importance of certain ongoing clinical trials and other emerging information, published abstracts were cited when they were the only published information available.

2008 Addendum

The writing committee reviewed the results of trials that were published after the 2006 recommendations were issued.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials

Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies

Level of Evidence C: Expert opinion or case studies

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A writing committee chair and vice chair were designated by the Stroke Council Manuscript Oversight Committee. A writing committee roster was developed and approved by the Stroke Council with representatives from neurology, cardiology, radiology, surgery, nursing, and health services research. The committee met in person and had a number of teleconferences to develop the outline and text of the recommendations.

All members of the committee had frequent opportunities to review drafts of the document, comment in writing or during teleconference discussions, and reach consensus with the final recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Class I: Conditions for which there is evidence and/or general agreement that the procedure or treatment is useful and effective

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment

> **Class IIa**: Weight of evidence or opinion is in favor of the procedure or treatment.
>
> **Class IIb**: Usefulness/efficacy is less well established by evidence or opinion.

Class III: Conditions for which there is evidence and/or general agreement that a procedure or treatment is not useful/effective and in some cases may be harmful

COST ANALYSIS

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Expert peer review of American Heart Association (AHA) Scientific Statements is conducted at the AHA National Center. For more on AHA statements and guidelines development, visit http://www.americanheart.org/presenter.jhtml?identifier=3023366.

2006 Guideline

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on September 16, 2005.

2008 Addendum

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on January 11, 2008.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the American Heart Association/American Stroke Association (AHA/ASA)*: The AHA/ASA Writing committee for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack (TIA) has reviewed the results of recent trials that were published after their previous recommendations were issues. The 2 areas in which major new clinical trials have been published are (1) the use of specific antiplatelet agents for stroke prevention in patients with a history of noncardioembolic ischemic stroke or TIA and (2) the use of statins in the prevention of recurrent stroke. Recommendations that have been changed since the original 2006 guideline are followed by the label* ***(2008 Addendum)****.*

Definitions for the weight of the evidence (A-C) and classes of recommendations (I-III) are provided at the end of the "Major Recommendations" field.

Abbreviations used in the tables are also listed at the end of the "Major Recommendations" field.

Recommendations for Treatable Vascular Risk Factors

Risk Factor	Recommendation	Class/Level of Evidence
Hypertension	Antihypertensive treatment is recommended for prevention of recurrent stroke and other vascular events in persons who have had an ischemic stroke and are beyond the hyperacute period.	Class I, Level A
	Because this benefit extends to persons with and without a history of hypertension, this recommendation should be considered for all ischemic stroke and TIA	Class IIa, Level B

Risk Factor	Recommendation	Class/Level of Evidence
	patients.	
	An absolute target BP Level and reduction are uncertain and should be individualized, but benefit has been associated with an average reduction of approximately 10/5 mm Hg and normal BP levels have been defined as <120/80 by JNC-7.	Class IIa, Level B
	Several lifestyle modifications have been associated with BP reductions and should be included as part of a comprehensive approach antihypertensive therapy.	Class IIb, Level C
	Optimal drug regimen remains uncertain; however, available data support the use of diuretics and the combination of diuretics and an ACEI. Choice of specific drugs and targets should be individualized on the basis of reviewed data and consideration, as well as specific patient characteristics (e.g., extracranial cerebrovascular occlusive disease, renal impairment, cardiac disease, and DM).	Class I, Level A
Diabetes	More rigorous control of blood pressure and lipids should be considered in patients with diabetes.	Class IIa, Level B
	Although all major classes of antihypertensives are suitable for the control of BP, most patients will require >1 agent. ACEIs and ARBs are more effective in reducing the progression of renal disease and are recommended as first-choice medications for patients with DM.	Class I, Level A
	Glucose control is recommended to near-normoglycemic levels among diabetics with ischemic stroke or TIA to reduce microvascular complications.	Class I, Level A
	The goal for Hb A1c should be $\leq$7%.	Class IIa, Level B
Cholesterol	Ischemic stroke or TIA patients with elevated cholesterol, comorbid CAD, or evidence of an atherosclerotic origin should be managed according to NCEP III guidelines, which include lifestyle modification, dietary guidelines, and medication recommendations.	Class I, Level A
	Statin agents are recommended, and the target goal for cholesterol lowering for those with CHD or symptomatic atherosclerotic disease is an LDL-C of <100 mg/dL. An LDL-C <70 mg/dL is recommended for very-high-risk persons with multiple risk factors.	Class I, Level A
	On the basis of the SPARCL trial, administration of statin therapy with intensive lipid-lowering effects is recommended for patients with atherosclerotic ischemic stroke or TIA and without known CHD to reduce the risk of stroke and cardiovascular events. **(2008**	Class I, Level B

Risk Factor	Recommendation	Class/Level of Evidence
	Addendum)	
	Ischemic stroke or TIA patients with low HDL cholesterol may be considered for treatment with niacin or gemfibrozil.	Class IIb, Level B

Recommendations for Modifiable Behavioral Risk Factors

Risk Factor	Recommendation	Class/Level of Evidence
Smoking	All ischemic stroke or TIA patients who have smoked in the past year should be strongly encouraged not to smoke.	Class I, Level C
	Avoid environmental smoke.	Class IIa, Level C
	Counseling, nicotine products, and oral smoking cessation medications have been found to be effective for smokers.	Class IIa, Level B
Alcohol	Patients with prior ischemic stroke or TIA who are heavy drinkers should eliminate or reduce their consumption of alcohol.	Class I, Level A
	Light to moderate levels of $\leq$2 drinks per day for men and 1 drink per day for nonpregnant women may be considered.	Class IIb, Level C
Obesity	Weight reduction may be considered for all overweight ischemic stroke or TIA patients to maintain the goal of a BMI of 18.5 to 24.9 kg/m^2 and a waist circumference of <35 inches for women and <40 inches for men. Clinicians should encourage weight management through an appropriate balance of caloric intake, physical activity, and behavioral counseling.	Class IIb, Level C
Physical activity	For those with ischemic stroke or TIA who are capable of engaging in physical activity, at least 30 minutes of moderate-intensity physical exercise most days may be considered to reduce risk factors and comorbid conditions that increase the likelihood of recurrence of stroke. For those with disability after ischemic stroke, a supervised therapeutic exercise regimen is recommended.	Class IIb, Level C

Recommendations for Interventional Approaches to Patients With Stroke Caused by Large-Artery Atherosclerotic Disease

Risk Factor	Recommendation	Class/Level of Evidence
Extracranial carotid disease	For patients with recent TIA or ischemic stroke within the last 6 months and ipsilateral severe (70 to 99%) carotid artery stenosis, CEA is recommended by a surgeon with a perioperative	Class I, Level A

Risk Factor	Recommendation	Class/Level of Evidence
	morbidity and mortality of <6%.	
	For patients with recent TIA or ischemic stroke and ipsilateral moderate (50 to 69%) carotid stenosis, CEA is recommended, depending on patient-specific factors such as age, gender, comorbidities, and severity of initial symptoms.	Class I, Level A
	When degree of stenosis is <50%, there is no indication for CEA.	Class III, Level A
	When CEA is indicated, surgery within 2 weeks rather than delayed surgery is suggested.	Class IIa, Level B
	Among patients with symptomatic severe stenosis (>70%) in whom the stenosis is difficult to access surgically, medical conditions are present that greatly increase the risk for surgery, or when other specific circumstances exist such as radiation-induced stenosis or restenosis after CEA, CAS is not inferior to endarterectomy and may be considered.	Class IIb, Level B
	CAS is reasonable when performed by operators with established periprocedural morbidity and mortality rates of 4 to 6%, similar to that observed in trials of CEA and CAS.	Class IIa, Level B
	Among patients with symptomatic carotid occlusion, EC/IC bypass surgery is not routinely recommended.	Class III, Level A
Extracranial vertebrobasilar disease	Endovascular treatment of patients with symptomatic extracranial vertebral stenosis may be considered when patients are having symptoms despite medical therapies (antithrombotics, statins, and other treatments for risk factors).	Class IIb, Level C
Intracranial arterial disease	The usefulness of endovascular therapy (angioplasty and/or stent placement) is uncertain for patients with hemodynamically significant intracranial stenoses who have symptoms despite medical therapies (antithrombotics, statins, and other treatments for risk factors) and is considered investigational.	Class IIb, Level C

Recommendations for Patients with Cardioembolic Stroke Types

Risk Factor	Recommendation	Class/Level of Evidence
AF	For patients with ischemic stroke or TIA with persistent or paroxysmal (intermittent) AF, anticoagulation with adjusted-dose warfarin (target INR, 2.5; range, 2.0-3.0) is recommended.	Class I, Level A

Risk Factor	Recommendation	Class/Level of Evidence
	In patients unable to take oral anticoagulants, aspirin 325 mg/d is recommended.	Class I, Level A
Acute MI and LV thrombus	For patients with an ischemic stroke caused by an acute MI in whom LV mural thrombus is identified by echocardiography or another form of cardiac imaging, oral anticoagulation is reasonable, aiming for an INR of 2.0 to 3.0 for at least 3 months and up to 1 year.	Class IIa, Level B
	Aspirin should be used concurrently for the ischemic CAD patient during oral anticoagulant therapy in doses up to 162 mg/d, preferably in the enteric-coated form.	Class IIa, Level A
Cardiomyopathy	For patients with ischemic stroke or TIA who have dilated cardiomyopathy, either warfarin (INR, 2.0 to 3.0) or antiplatelet therapy may be considered for prevention of recurrent events.	Class IIb, Level C
Valvular heart disease		
Rheumatic mitral valve disease	For patients with ischemic stroke or TIA who have rheumatic mitral valve disease, whether or not AF is present, long-term warfarin therapy is reasonable, with a target INR of 2.5 (range, 2.0-3.0).	Class IIa, Level C
	Antiplatelet agents should not be routinely added to warfarin in the interest of avoiding additional bleeding risk.	Class III, Level C
	For ischemic stroke or TIA patients with rheumatic mitral valve disease, whether or not AF is present, who have a recurrent embolism while receiving warfarin, adding aspirin (81 mg/d) is suggested.	Class IIa, Level C
MVP	For patients with MVP who have ischemic stroke or TIAs, long-term antiplatelet therapy is reasonable.	Class IIa, Level C
MAC	For patients with ischemic stroke or TIA and MAC not documented to be calcific, antiplatelet therapy may be considered.	Class IIb, Level C
	Among patients with mitral regurgitation resulting from MAC without AF, antiplatelet or warfarin therapy may be considered.	Class IIb, Level C
Aortic valve disease	For patients with ischemic stroke or TIA and aortic valve disease who do not have AF, antiplatelet therapy may be considered.	Class IIa, Level C
Prosthetic heart valves	For patients with ischemic stroke or TIA who have modern mechanical prosthetic heart valves, oral anticoagulants are recommended, with an INR target of 3.0 (range, 2.5-3.5).	Class I, Level B
	For patients with mechanical prosthetic heart	Class IIa,

Risk Factor	Recommendation	Class/Level of Evidence
	valves who have an ischemic stroke or systemic embolism despite adequate therapy with oral anticoagulants, aspirin 75 to 100 mg/d, in addition to oral anticoagulants, and maintenance of the INR at a target of 3.0 (range, 2.5-3.5) is reasonable.	Level B
	For patients with ischemic stroke or TIA who have bioprosthetic heart valves with no other source of thromboembolism, anticoagulation with warfarin (INR, 2.0-3.0) may be considered.	Class IIb, Level C

Recommendations for Antithrombotic Therapy for Noncardioembolic Stroke or TIA (Oral Anticoagulant and Antiplatelet Therapies)

Recommendation	Class/Level of Evidence
For patients with noncardioembolic ischemic stroke or TIA, antiplatelet agents rather than oral anticoagulation are recommended to reduce the risk of recurrent stroke and other cardiovascular events.	Class I, Level A
Aspirin (50 to 325 mg/d) monotherapy, the combination of aspirin and extended-release dipyridamole, and clopidogrel monotherapy are all acceptable options for initial therapy.* **(2008 Addendum)**	Class I, Level A
The combination of aspirin and extended-release dipyridamole is recommended over aspirin alone. **(2008 Addendum)**	Class I, Level B
Clopidogrel may be considered over aspirin alone on the basis of direct-comparison trials.	Class IIb, Level B
For patients allergic to aspirin, clopidogrel is reasonable.	Class IIa, Level B
The addition of aspirin to clopidogrel increases the risk of hemorrhage. Combination therapy of aspirin and clopidogrel is not routinely recommended for ischemic stroke or TIA patients unless they have a specific indication for this therapy (i.e., coronary stent or acute coronary syndrome).	Class III, Level A

*For patients who have an ischemic cerebrovascular event while taking aspirin, there is no evidence that increasing the dose of aspirin provides additional benefit. Although alternative antiplatelet agents are often considered for noncardioembolic patients, no single agent or combination has been well studied in patients who have had an event while receiving aspirin.

Recommendations for Stroke Patients With Other Specific Conditions

Risk Factor	Recommendation	Class/Level of Evidence
Arterial dissection	For patients with ischemic stroke or TIA and arterial dissection, warfarin for 3 to 6 months or antiplatelet agents are	Class IIa, Level B

Risk Factor	Recommendation	Class/Level of Evidence
	reasonable.	
	Beyond 3 to 6 months, long-term antiplatelet therapy is reasonable for most ischemic stroke or TIA patients. Anticoagulant therapy beyond 3 to 6 months may be considered among patients with recurrent ischemic events.	Class IIb, Level C
	For patients who have definite recurrent ischemic events despite antithrombotic therapy, endovascular therapy (stenting) may be considered.	Class IIb, Level C
	Patients who fail or are not candidates for endovascular therapy may be considered for surgical treatment.	Class IIb, Level C
Patent foramen ovale	For patients with an ischemic stroke or TIA and a PFO, antiplatelet therapy is reasonable to prevent a recurrent event.	Class IIa, Level B
	Warfarin is reasonable for high-risk patients who have other indications for oral anticoagulation such as those with an underlying hypercoagulable state or evidence of venous thrombosis.	Class IIa, Level C
	Insufficient data exist to make a recommendation about PFO closure in patients with a first stroke and a PFO. PFO closure may be considered for patients with recurrent cryptogenic stroke despite medical therapy.	Class IIb, Level C
Hyperhomocysteinemia	For patients with an ischemic stroke or TIA and hyperhomocysteinemia (levels >10 micromol/L), daily standard multivitamin preparations are reasonable to reduce the level of homocysteine, given their safety and low cost. However, there is no evidence that reducing homocysteine levels will lead to a reduction of stroke occurrence.	Class I, Level A
Hypercoagulable states		
Inherited thrombophilias	Patients with an ischemic stroke or TIA with an established inherited thrombophilia should be evaluated for deep venous thrombosis, which is an indication for short- or long-term anticoagulant therapy, depending on the clinical and hematologic circumstances.	Class IIa, Level A
	Patients should be fully evaluated for alternative mechanisms of stroke.	Class IIa, Level C

Risk Factor	Recommendation	Class/Level of Evidence
	In the absence of venous thrombosis, long-term anticoagulation or antiplatelet therapy is reasonable.	
	Patients with a history of recurrent thrombotic events may be considered for long-term anticoagulation.	Class IIb, Level C
Antiphospholipid antibody syndrome	For cases of cryptogenic ischemic stroke or TIA and positive APL antibodies, antiplatelet therapy is reasonable.	Class IIa, Level B
	For patients with ischemic stroke or TIA who meet the criteria for the APL antibody syndrome with venous and arterial occlusive disease in multiple organs, miscarriages, and livedo reticularis, oral anticoagulation with a target INR of 2 to 3 is reasonable.	Class IIa, Level B
Sickle-cell disease	For adults with SCD and ischemic stroke or TIA, general treatment recommendations cited above are applicable with regard to the control of risk factors and use of antiplatelet agents.	Class IIa, Level B
	Additional therapies that may be added include regular blood transfusion to reduce Hb S to <30 to 50% of total Hb, hydroxyurea, or bypass surgery in cases of advanced occlusive disease.	Class IIb, Level C
Cerebral venous sinus thrombosis	For patients with cerebral venous sinus thrombosis, UFH or LMWH is reasonable even in the presence of hemorrhagic infarction.	Class IIa, Level B
	Continuation of anticoagulation with an oral anticoagulant agent is reasonable for 3 to 6 months, followed by antiplatelet therapy.	Class IIa, Level C
Pregnancy	For pregnant women with an ischemic stroke or TIA and high-risk thromboembolic conditions such as known coagulopathy or mechanical heart valves, the following options may be considered: • Adjusted-dose UFH throughout pregnancy such as a subcutaneous dose every 12 h with APTT monitoring • Adjusted-dose LMWH with factor Xa monitoring throughout pregnancy • UFH or LMWH until week 13, followed by warfarin until the middle of the third trimester, when UFH or LMWH is	Class IIb, Level C

Risk Factor	Recommendation	Class/Level of Evidence
	then reinstituted until delivery.	
	Pregnant women with lower-risk conditions may be considered for treatment with UFH or LMWH in the first trimester, followed by low-dose aspirin for the remainder of the pregnancy.	Class IIb, Level C
Postmenopausal HRT	For women with stroke or TIA, postmenopausal HRT is not recommended.	Class III, Level A
Cerebral hemorrhage	For patients who develop an ICH, SAH, or SDH, all anticoagulants and antiplatelets should be discontinued during the acute period for at least 1 to 2 weeks after the hemorrhage and the anticoagulant effect reversed immediately with appropriate agents (i.e., vitamin K, FFP).	Class III, Level B
	For patients who require anticoagulation soon after a cerebral hemorrhage, intravenous heparin may be safer than oral anticoagulation. Oral anticoagulants may be resumed after 3 to 4 weeks, with rigorous monitoring and maintenance of INRs in the lower end of the therapeutic range.	Class IIb, Level C
	Special circumstances:	
	Anticoagulation should not be resumed after an SAH until the ruptured aneurysm is definitively secured.	Class III, Level C
	Patients with lobar ICHs or microbleeds and suspected CAA on MRI may be at a higher risk for recurrent ICH if anticoagulation needs to be resumed.	Class IIb, Level C
	For patients with hemorrhagic infarction, anticoagulation may be continued, depending on the specific clinical scenario and underlying indication for anticoagulant therapy.	Class IIb, Level C

Recommendations for Special Approaches for Implementing Guidelines and Their Use in High-Risk Populations

- To prevent underutilization or disparities in the use of therapies recommended in national guidelines, the guideline development and distribution process should recognize and incorporate strategies for increased implementation **(Class I, Level of Evidence B)**.
- It is reasonable that intervention strategies emphasize improved access to care for the aged, underserved, and ethnic populations by addressing

economic barriers (e.g., coverage for services required), geographic barriers (e.g., expanded use of telemedicine), and a multidisciplinary approach to increase patient and healthcare provider compliance with guidelines and practice parameters **(Class IIa, Level of Evidence B)**.

Abbreviations:

ACEI, angiotensin-converting enzyme inhibitor
AF, atrial fibrillation
APL, antiphospholipid
APTT, activated partial thromboplastin time
ARB, angiotensin receptor blocker
BMI, body mass index
BP, blood pressure
CAA, cerebral amyloid angiopathy
CAD, coronary artery disease
CAS, carotid artery balloon angioplasty and stenting
CEA, carotid endarterectomy
CHD, coronary heart disease
DM, diabetes mellitus
EC/IC, extracranial-intracranial
FFP, fast frozen plasma
Hb A1c, hemoglobin A1c (glycosylated hemoglobin)
Hb S, hemoglobin S formation
HDL-C, high-density lipoprotein-cholesterol
HRT, hormone replacement therapy
ICH, intracerebral hemorrhage
INR, international normalized ratio
JNC-7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure
LDL-C, low-density lipoprotein-cholesterol
LMWH, low-molecular weight heparin
LV, left ventricular
MAC, mitral annular calcification
MI, myocardial infarction
MRI, magnetic resonance imaging
MVP, mitral valve prolapse
NCEP, National Cholesterol Education Program
PFO, patent foramen ovale
SAH, subarachnoid hemorrhage
SCD, sickle-cell disease
SDH, subdural hematoma
SPARCL, Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial
TIA, transient ischemic attack
UFH, unfractionated heparin

Definitions:

Levels of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials

Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies

Level of Evidence C: Expert opinion or case studies

Strength of Recommendations

Class I: Conditions for which there is evidence and/or general agreement that the procedure or treatment is useful and effective

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment

Class IIa: Weight of evidence or opinion is in favor of the procedure or treatment.

Class IIb: Usefulness/efficacy is less well established by evidence or opinion.

Class III: Conditions for which there is evidence and/or general agreement that a procedure or treatment is not useful/effective and in some cases may be harmful

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Reduced risk of stroke, myocardial infarction, and mortality

POTENTIAL HARMS

Adverse Effects of Medications

- *Warfarin* use has been shown to be relatively safe, with annual rate of major bleeding of 1.3% for patients on warfarin compared with 1% for patients on placebo or aspirin. The narrow therapeutic margin of *warfarin* in conjunction with numerous associated food and drug interactions requires frequent international normalized ratio (INR) testing and dose adjustments. These liabilities of *warfarin* contribute to significant underutilization, even in high-

risk patients. *Warfarin* is not usually recommended during pregnancy primarily because of concerns of fetal safety, but it is an option identified by the American College of Chest Physicians (ACCP).

- Higher doses of *aspirin* (1200 versus 300 mg/d and 283 versus 30 mg/d) have been associated with a greater risk of gastrointestinal hemorrhage
- The most common side effects of *ticlopidine* are diarrhea (~12%), other gastrointestinal symptoms, and rash, with a frequency of hemorrhagic complications similar to that of aspirin. Neutropenia occurred in ~2% of patients treated with *ticlopidine*; however, it was severe in <1% and was almost always reversible with discontinuation. Thrombotic thrombocytopenic purpura has also been described.
- The safety of *clopidogrel* is comparable to that of aspirin, and it has clear advantages over ticlopidine. As with ticlopidine, diarrhea and rash are more frequent than with aspirin, but gastrointestinal symptoms and hemorrhages are less frequent. Neutropenia is not a problem with *clopidogrel*, but a few cases of thrombotic thrombocytopenic purpura have been described.
- Headache is the most common side effect of extended-release *dipyridamole*. Bleeding was not significantly increased by *dipyridamole*. Although there are concerns about the use of immediate-release *dipyridamole* in patients with stable angina, a post hoc analysis from ESPS-2 that used extended-release *dipyridamole* showed no excess of adverse cardiac events compared with placebo or aspirin.
- *Combination of clopidogrel and aspirin* was associated with significantly increased risk of major hemorrhage compared with clopidogrel alone, with 1.3% absolute increase in life-threatening bleeding.
- The risk of *heparin* causing hemorrhagic transformation in patients with arterial dissection appears low (<5%).
- *Surgical therapy* in patients with arterial dissection has been associated with complication rates of at least 10% to 12% (stroke and death combined), which are higher than those reported with medical therapy alone.
- Elevation in liver enzymes was more common (2.2% versus 0.5%) and creatine kinase was more frequent (0.1% versus 0%) with *atorvastatin* treatment.

CONTRAINDICATIONS

CONTRAINDICATIONS

Use of *heparin* or other anticoagulants in patients with a subarachnoid hemorrhage related to a dissection is contraindicated.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Systematic approaches to guideline implementation are needed to overcome the barriers to effective use by healthcare professionals. This was recognized by the authors of the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) who stated: Although traditional continuing medical education (CME) programs that use lectures and conferences to teach physicians rarely change professional practice, they can

increase awareness and motivate physicians to learn more specific approaches to therapy. Moreover, when physician-training programs supply important background material (i.e., science) and guidance on ways to implement treatment guidelines into everyday practice, they are more likely to influence practice. For example, when training programs provide the physician with enabling strategies (e.g., office reminders), reinforcing strategies (e.g., feedback), and predisposing strategies (e.g., practice guidelines), improvements in the quality of practice are more commonly seen.

An American Heart Association (AHA) pilot program to improve post-myocardial infarction (MI) implementation of coronary artery disease secondary prevention (Get With the Guidelines-CAD) demonstrated substantial improvements in care. The program uses a collaborative model embedded in a systems approach that includes online access to relevant guidelines, preprinted and discharge order sets, and physician reminders to achieve increases in smoking cessation counseling from 53% to 88% ($P<0.05$), lipid therapy at discharge from 54% to 78% ($P<0.05$), and referral to cardiac rehabilitation from 33% to 73% ($P<0.05$) over a 1-year period.

The National Institutes of Health (NIH) has recognized the treatment gap between clinically proven therapies and actual treatment rates in the community and has created a new Roadmap for Medical Research to reengineer clinical research and "remove some of the biggest roadblocks that are keeping research findings from reaching the public as swiftly as possible." To ensure that scientific knowledge is translated effectively into practice and that healthcare disparities are addressed, the Institute of Medicine of the National Academy of Sciences has recommended the establishment of coordinated systems of care that integrate preventive and treatment services and promote patient access to evidence-based care.

Guideline recommendations should be defined as explicitly as possible, with an eye toward how they will be interpreted in the care-delivery setting and in populations that differ from the original study populations. To remain relevant, these guidelines should be updated frequently so that they reflect the latest evidence-based consensus among experts. This process of updating guidelines should take into account information about levels of compliance with previously published guidelines and challenges to implementation. Implementation of guidelines offers a unique opportunity to identify and help address disparities in healthcare delivery. The science of guideline implementation and the methods available to facilitate behavior change among patients and physicians should be the subject of formal study by organizations that promulgate guidelines.

Identifying and Responding to Populations at Highest Risk

For the aged, socially disadvantaged, and specific ethnic groups, inadequate implementation of guidelines and noncompliance with prevention recommendations are critical problems. Expert panels have indicated the need for a multilevel approach to include the patient, provider, and organization delivering health care. The evidence for such is well documented, yet further research is sorely needed. The National Institute of Neurological Disease and Stroke (NINDS) Stroke Disparities Planning Panel, convened in June 2002, is developing strategies that include establishing data collection systems and exploring effective community impact programs and instruments in stroke prevention. Alliances with

the federal government through the NINDS, nonprofit organizations such as the AHA/American Stroke Association, and medical specialty groups such as the American Academy of Neurology and the Brain Attack Coalition to coordinate, develop, and enhance such strategies are continuing in a more focused fashion. Finally, patients are becoming more effective advocates for stroke prevention through community awareness programs. The NINDS report of the Stroke Progress Review Group serves as a framework for stroke research over this decade and joins the federal government's Healthy People 2010 and the AHA/American Stroke Association strategic goal to significantly reduce stroke and those at risk for stroke by the year 2010.

See also "Recommendations for Special Approaches for Implementing Guidelines and Their Use in High-Risk Populations" in the "Major Recommendations" field.

IMPLEMENTATION TOOLS

Tool Kits

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Adams RJ, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Sacco RL, Schwamm LH, American Heart Association, American Stroke Association. Update to the AHA/ASA recommendations for the prevention of stroke in patients with stroke and transient ischemic attack. Stroke 2008 May;39(5):1647-52. [10 references] PubMed

Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke

Association Council on Stroke [trunc]. Stroke 2006 Feb;37(2):577-617. [466 references] PubMed

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American Heart Association/American Stroke Association (AHA/ASA) Writing Committee for the Prevention of Stroke in Patient With Stroke and Transient Ischemic Attack (TIA)

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

Table: 2008 Addendum Writing Group Disclosures (for the original 2006 disclosures, see full text of the 2006 guideline document)

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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12 month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

**Significant.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

2006 Guideline

Electronic copies: Available from the American Heart Association Web site.

2008 Addendum

Electronic copies: Available from the American Heart Association Web site.

Print copies: Available from the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596; Phone: 800-242-8721

AVAILABILITY OF COMPANION DOCUMENTS

Get With the Guidelines (GWTG) provides disease-specific process documents and tools for in-house quality improvement. See the American Heart Association Web site for more information. See the related QualityTool summary on the Health Care Innovations Exchange Web site for this related tool set.

PATIENT RESOURCES

None available

NGC STATUS

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